COMPUTER ASSISTED MEASUREMENTS AND GRAPHICAL DISPLAY TECHNIQUES IN CLINICAL NEUROPHYSIOLOGY
– five applications

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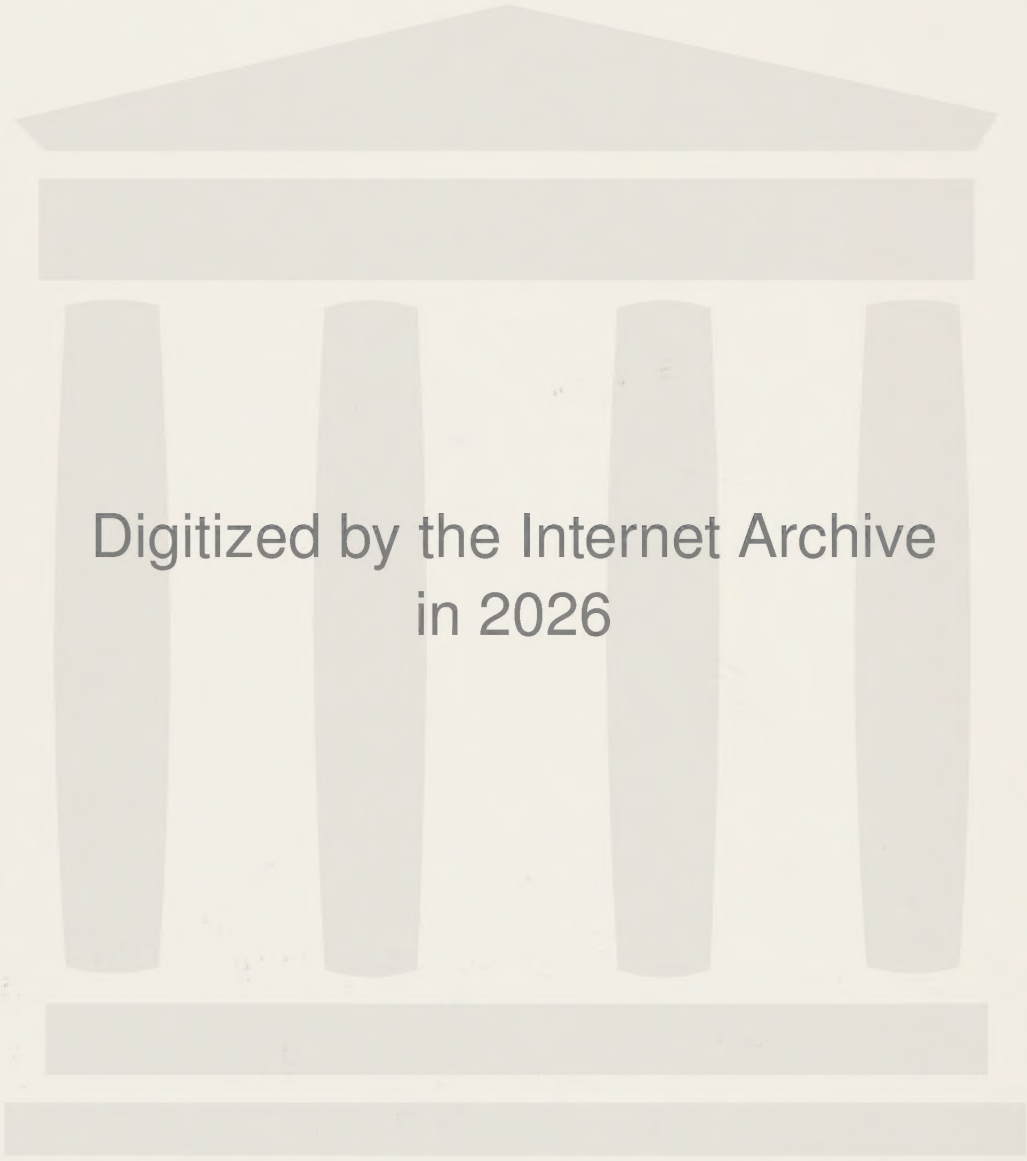
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1 INTRODUCTION

Neuroscience has a long tradition of employing various measurement techniques, clinically as well as in animal and in vitro experiments. The most well known is perhaps the electroencephalogram - EEG or electrical 'brain waves'.

In the early history of neurophysiology, the measurements consisted simply of recording different electrical activity in the nervous system. The analysis of such recordings, including EEG, was done on a purely qualitative basis, directly by the human investigator.

During the last decades even other measuring methods have come into use (e.g. scintigraphy, ultrasound, and x-rays). At the same time quantitative methods of evaluating the data have been developed. Since computers have become available the practical possibilities of doing more sophisticated measurements even clinically have increased remarkably (cf. Karshmer et al. 1978).

Especially for use in clinical routine computer based measurement equipment offers certain advantages. Except for the possibilities of making both measurements and extensive calculations in real time, the computer makes it possible to adapt the result presentation, and operator communication to the various needs of the laboratory situation. Also much of the documentation needed for each clinical investigation may conveniently be maintained by such systems.

This thesis summarises five different applications of computer assisted measurements in clinical neurophysiology. They have all been carried out in a clinical environment at Lund University Hospital, and in very close cooperation between clinically experienced medical doctors and engineers.

The thesis consists of the following papers which will be discussed below in more detail:

I. PHILIPSON L: Computer based systems for measurements, result calculations and graphical display of regional cerebral blood flow in man. Technical report. Dep of clinical neurophysiology, Lund university hospital, 1980.

II. INGVAR D H and PHILIPSON L: Distribution of cerebral blood flow in the dominant hemisphere during motor ideation and motor performance. Ann Neurol 2(3), 230-237, 1977.

III. PHILIPSON L, RISBERG A-M and INGVAR D H: Normal sleep pattern analyzed statistically and studied by 'dormograms' in colour. Accepted for publication in Sleep.

IV. PHILIPSON L: Software development on the EMI head scanner. Comp Prog Biomed 10, 162-171, 1979.

V. PHILIPSON L: Computer analysis of motor unit discharge patterns. In: Anderson J (ed): Proceedings from Medical Informatics Europe 78, Cambridge, England 1978, Springer Verlag, 1978, pp 555-563.

In the text, these papers will be referred to by their Roman numerals.

2 COMMENTS ON THE PAPERS

2.1 Regional blood flow measurements (paper I)

The first quantitative determination of regional blood flow (rCBF) in man was achieved by Ingvar and Lassen in 1961 (Ingvar et al. 1961). Previous methods permitted only a determination of the average blood flow of the brain as a whole. Regional measurements made it possible to detect, in a quantitative way, the local variations of cerebral blood flow caused e.g. by vascular disorders. Later it turned out that the distribution of blood flow may change also in normal brains due to different physiological and even mental states, reflecting the different distributions of cerebral activity and metabolism.

The method introduced by Ingvar and Lassen, and other that followed, have given rise to a discipline of its own in brain science. International conferences on cerebral blood flow and metabolism are now being held regularly every two years, the ninth in this series last year in Tokyo (Gotoh 1979).

After having evaluated the physiological possibilities of the new method, technical refinement started. One of the main lines was to increase the spatial resolution of the regional measurements, which was accomplished by using multidetector systems with ever increasing number of detectors. At the same time, more sophisticated mathematical methods were developed to elicit more information from the measurements, which in turn required better calculation facilities for evaluation of the results.

When the first minicomputers entered the scene in the middle of the sixties, it became obvious that computer technology was going to be the key to multi-detector systems with real time calculation and result display capability.

Paper I describes the development of a computer-based multi detector system for on-line measurement, calculation and display of rCBF. Ex-

cept for all the design details specific for the application, the project included two main parts of a more general interest. The first one concerned general design principles for high level language programming of a real time measurement system with command handling and display facilities, implemented on a minicomputer. Secondly, the project involved an evaluation of different graphical display techniques and development of a powerful basic software package for a sophisticated graphical display device. These parts of the project are discussed in some more detail in section 3 below.

For certain reasons, paper I contains a far more detailed technical description of the system in case that the rest of the papers. One reason is that it is an internal report, while the others were written to be published in various journals. Even technically oriented journals have rather strong limits on the amount of implementation details that may be included in a paper, and in medical journals technical details are even less favoured. Another reason for having made a detailed report on this first project is that it also serves as the only complete technical documentation of that system. This report may be regarded as an example of how projects were carried out in detail, valid also for the other projects.

2.2 Cerebral ideograms in colour (paper II)

Individual measurements of regional blood flow by the method described in paper I may be presented as coarse maps of blood flow distribution over the cerebral hemisphere. Having done a series of measurements under similar conditions, the problem arises of presenting the result in a comprehensive form that emphasizes the common features and disregards stochastical variations.

In paper II a computer based method was used to produce colour coded maps representing smoothed, two-dimensional averages of a number of flow maps from series of individual blood flow measurements. These maps have been termed 'cerebral ideograms' since they reveal the cor-

relation between blood flow and mental states (according to Encyclopedia Britannica an 'ideogram' is defined as 'a pictorial display that conveys an idea').

The amount of computations required to produce a single ideogram is so large that it is quite impossible to carry out without a computer. This reflects the fact that the ideogram is not a mere superposition of individual maps, but a spatial average that takes into account also details of the pattern in the neighbourhood of each position in all the ingoing flow maps.

The technical background and the programs for producing the ideograms are presented in paper I (Appendix B). Originally the technique was designed to be used together with the ink jet hard copy colour display system at the Lund University Computing Center. After having included a colour-TV display processor in the laboratory computer system, the technique was implemented also on that one. This gave direct access to the method in the laboratory, which was very important both for the further development of the method and for the practical use of it.

At the time the ideogram technique was developed (early spring of 1976) to our knowledge there was no similar method in use for the same purpose anywhere else. Later the cerebral blood flow group in Copenhagen has adopted a display technique where a number of flow maps from individual measurements are superimposed, which yields results of the same nature as the ideograms (Lassen et al. 1977).

Paper II was the first presentation of cerebral ideograms that was written, but not the first one to be published. By now cerebral ideograms have been used in a number of papers (Blanc 1976, Philipson et al. 1977, 1978, Ingvar 1976, 1978a,b, 1979, Ingvar et al. 1977, 1978, 1979).

2.3 Sleep data base and dormograms in colour (paper III)

Polygraphic sleep studies are based on continuous recording of different physiological parameters such as the electrical mass activity in the brain (EEG), the (electrical) activity in muscles (EMG), eye movements (EOC), heart beat (ECG), respiration, blood pressure and body movements. During each 30-second period of an investigation a full page of graph recordings of the different parameters is produced. For a whole night this results in a substantial amount of data. There is however yet no reliable method for automatic evaluation of such data. Even after visual evaluation of the sleep stage for each page of the recording (Wake - REM - 1 - 2 - 3+4), a lot of data handling and manipulation remain in order to evaluate and display the sleep patterns of a complete study, normally consisting of a series of nights.

Paper III describes a project where computer technique was used to store, retrieve, make calculations on, and display such data. After the visual evaluation, the sleep stage data were manually fed into a computer and stored together with some basic data on the patient etc. in a very simple data base on magnetic tape. The philosophy behind this was to store all relevant data about each night on a computer-accessible medium, at the earliest possible stage of the evaluation process. The appropriate stage for this is immediately after the visual evaluation of the polygraphic recordings. Once all the data are stored in a form where they are readily accessible for the computer, all sorts of programs for sleep data evaluation, statistical calculations and graphical displays of sleep patterns may be developed.

Several such functions were implemented in this project, both for handling single nights and groups of nights. The sleep curve of each night might be presented graphically together with some statistical data on the distribution of sleep stages during the night. Furthermore, a set of internationally standardized sleep parameters might be automatically calculated and stored in a secondary, smallar data base on a magnetic disk, more suitable for interactive selection of groups of nights. This secondary data base might then be used to

select suitable subgroups of nights on the basis of logical search-keys. The sleep parameters of such a subgroup might then be analyzed statistically and compared to the parameters of another group in order to find significant relations.

In order to visualize the typical sleep pattern in a series of nights, a technique very similar to the ideogram technique (paper II) was developed. The resulting images - dormograms in colour - show the statistical distribution of sleep stages during the night in the whole group. By choosing an appropriate colour scale, the 'majority pattern' may easily be recognized by the observer. Such dormograms may be used to give an intuitive basis for further quantitative analysis of the data.

All software for handling the two sleep data bases and producing the different displays was designed in a general way to make it useful for handling both data from series of nights included in different research projects and from individual nights in clinical cases. The first project in which the system was used is the one reported in paper III, a study of normal sleep patterns in young, healthy volunteers. One of the results of this study was the reconstruction of a hypothetical mean sleep pattern, which may be used as a reference when evaluating individual nights of normal or pathological sleep.

The system has also been used in an extensive sleep study on hospital night workers, from which some preliminary results have already been reported (Risberg et al. 1979).

2.4 Further processing of tomographic images (paper IV)

Computerized tomography (CT) is a method to obtain x-ray images of cross-sections, 'slices', of the body. The first commercial CT-scanner was developed by EMI Ltd, and was introduced in 1972. Its impact on radiological diagnostics has already become so obvious, that it has been called the most important invention in the field since Röntgen's discovery in 1895.

The basis for this new technique is to make x-ray recordings from a number of different angles around the object and then use a computer to reconstruct the actual two-dimensional absorption distribution in a slice of the patient. Thus, the final image (tomogram) is the product of a computer program, a digital image, consisting of small picture elements, pixels, each associated with a number expressing the absorption of the corresponding volume element, voxel, of the slice. Such images may then be displayed on a video-screen and stored on various media such as magnetic disks or tapes.

One of the first machines of the new EMI head scanner CT1010 was installed at the Neurodialogy Department, Lund University Hospital, in 1977. The software package of that machine contained only the primary image reconstruction and display functions, but not further evaluation of the tomograms. Paper IV describes a project with the aim of extending the software of the scanner to include also some further processing of the tomographic images, such as subtraction, smoothing, magnification, vertical reconstructions and density profile display.

As the computer of the scanner, including all its software, was delivered as a 'black box', one of the main tasks of this project was to find out appropriate ways of getting into that box. EMI was willing to give out information on the data format on the disk, but not to make the source code of their programs available. The solution was then to install a standard operating system on the same disk as the scanner used for storing data, and to develop a separate program (EMILUND) that collects images from the disk, operates on them, and puts the results back in exactly the same format. In this way, the EMI software might handle these images in exactly the same way as if they had been original images. In order to make the new program appear as an integrated part of the system, its operator communication was designed to mimic that of the EMI software.

In a new version of their software package 4 (March, 1979), EMI has now included many of the features of EMILUND, except for the rather sophisticated curve-fitting allgorithm for the estimation of the inter-slice absorption distribution in vertical reconstructions.

2.5 Motor unit analysis (paper V)

A set of muscle fibers controlled by one single motor neuron in the spinal cord is called a motor unit (MU). The activity of these fibers will then always be synchronized by the firing of the motor neuron. A needle electrode in the vicinity of an active motor unit will pick up an electrical signal being a superposition of action potentials from the individual fibers. Due to differences in geometrical, electrical and physiological properties, the resulting signal will have different shapes for different motor units. For a constant position of the electrode, the shape of the potentials from each unit will be rather constant, while potentials from different units will have significantly different shapes. Potentials with different shapes may then be considered to come from different motor units.

An electromyographic (EMG) recording from a needle electrode in a muscle, usually contains a mixture of potentials from a number of active motor units. By volutary control of the contraction of the muscle, a recording containing potentials from only one or a few motor units may be obtained. In clinical practice commercially available EMG equipment is used, by which individual potentials may be recorded whenever the signal reaches an operator controlled trigger level. Several recorded potentials stored in a digital memory may then be displayed for visual inspection and evaluation by the operator. The clinically most relevant properties of motor unit potentials are their amplitude, duration and number of phases (number of peaks).

The project behind paper V started by a master's thesis work (Mandersson 1973) in which motor unit potentials from EMG recordings were identified and separated on the basis of their shapes. By averaging the individual potentials of each shape, each potential could be determined more reliably. The averaged potential were then used for automatic calculation of amplitude and duration. This procedure was made possible by digitizing the EMG signal and using a computer for the necessary calculations.

By this method, amplitude and duration values for a small number of motor unit potentials recorded in a mixed fashion could be obtained automatically. However, such a system does not provide any additional information about the units over conventional EMG equipment.

One of the properties of the motor units that cannot be studied by using conventional technique is the discharge pattern, i.e. the time course of firing for each unit. In paper V the motor unit separation method earlier developed for averaging was used to obtain information also about the discharge pattern for each motor unit. In this way it should be possible to obtain physiologically relevant information that usually is completely hidden to the investigator.

In order to evaluate the method, a system with on-line data acquisition and off-line calculation was developed. It was not fast enough to be used in clinical routine, but sufficiently convenient for performing small series of evaluations. The system was based on a general purpose minicomputer programmed in Fortran which provided convenient conditions for the necessary software development.

For an EMG signal containing potentials from several motor units, the separation process sometimes failed to recognize a potential, the shape of which had been distorted by overlapping by a potential from another unit. This kind of separation failures did not matter very much for obtaining averaged potentials, it only decreased the number of potentials contained in each average. In the case of discharge pattern analysis such failures will cause 'gaps' in the sequences, which will have severe effect on the results if no corrections are made for this effect.

The solution to this problem was inspired by a similar work on ECG recordings (Jonson et al. 1976). Automatical calculation of heart rate from an ECG signal is similar to the study of motor unit discharge patterns. However there exists a fundamental difference in that an EMG recording may contain potentials from several motor units while an ECG recording contains potentials from the heart only. However,

even in the case of ECG potentials, recognition failures may occur which cause artifacts in the calculated heart beat interval sequence.

A histogram of the intervals of such a sequence will contain one peak corresponding to the basic rate of the unit, and perhaps one or several other peaks corresponding to different kind of gaps in the sequence. Normally the main peak is dominant and easily recognizable. An automatic criterion for excluding the artifacts can be based upon accepting only the values within a certain percentile interval of the histogram. The mean value within that interval they may be used as a measure of the basic rate.

In the case of motor units the application of this method to some clinical data showed that the characteristic firing frequency of a motor during a certain degree of contraction may be a parameter of clinical value. Together with a display of the firing interval histogram, it conveys information about the temporal behaviour of the motor unit that is not possible to obtain with conventional technique.

The basic development and investigation of the method presented in paper V has been followed by an evaluation based on further clinical material (Hynninen 1979). It confirmed the impression that this kind of quantitative analysis may contribute to the clinical evaluation of EMG recordings. To make the method available for use in clinical routine, it must however be implemented to run in real time. A preliminary study has shown that this is possible to achieve by making extensive use of present microelectronic technology. As a master's thesis project, supervised by the author, the necessary hardware has now been integrated with a conventional EMG machine. It includes a microcomputer with a separate, high-speed arithmetical unit and graphical display facilities (Nilsson et al. 1980).

3 DESIGN OF COMPUTER BASED MEASUREMENT SYSTEMS

3.1 General

A computer based measurement system can include much more facilities than a measurement 'instrument' in the classical sense. Except for data aquisition ('measurement'), it may store data for future use, make extensive calculations in order e.g. to derive secondary quantities and desplay the results in various comprehensive ways, e.g. in graphical or pictorial form. Normally the whole procedure shall be carried out in real time under the control of a human operator. In that case the system must include some real time control and operator facilities.

The measurement systems described in this thesis were all designed to be used in a clinical environment. Therefore, the comments below about the different design principles are focused upon such systems. For applications of quite different kinds, e.g. industrial control systems, some of the comments may be less valid.

3.2 Data aquisition

On-line measurements most often involve some kind of sampling of analog or digital signals, controlled by internal (e.g. a real-time clock) or external events. In paper I the actual pulses to be recorded were counted by a peripheral device, and the counter values sampled by the computer. For high data rates, like in this example, such peripheral data aquisition devices may drastically reduce the load on the computer.

The system in paper V is another example. Here an analog signal was sampled with regular intervals and converted to digital values. However, in practice an intermediate data medium was used. The EMG signals were stored on an analog tape-recorder for later analysis. The main reason for this was that the calculations were too slow to

make the on-line investigation convenient to the patient. Another reason was that from the tape recording the same sequence might be analysed several times with different parameters which was very helpful in order to evaluate the program and the parameters.

3.3 Data bases

Two quite different kinds of data bases might be recognized in the type of systems described here. The first kind consists of a collection of measurement results, often stored on magnetic tape or disk. In papers III and IV the sleep stage data and the reconstructed tomograms are examples of such data bases. In paper I another such data base is described, consisting of rCBF results (CBFLIB). Except for calculated and derived quantities, also measured raw data may be included in such data bases. The magnetic tape version of the common data file (FLPOOL) in paper I is an example of a data base of that kind.

The reason for including these data bases in the different systems is the need for reexamination, redisplay or even recalculation of data from previous measurements. Once the data have been stored on a computer accessible medium, all sorts of data handling and manipulation can be conveniently made whenever necessary.

The other kind of data base consists of the set of run-time parameters, like calibration data etc., that must be available during the actual measurement procedure. Usually this data base is stored in the main memory of the computer during the measurement and data handling. A very pronounced example is the 'blank common' variables shared by all programs of the system presented in paper I. In that case, the data base and the programs interact in such intricate ways that they might be considered equally important components of the software. The programs of paper V contain a similar common variable data block holding parameters that control many of the fundamental features of the EMG analysis. Changing one of the fundamental parameters may effect

several parts of the programs and cause both the analysis and displays to change considerably.

Such run-time parameters may be initiated in the programs by the operator or by making some kind of initializing measurement (e.g. calibration or base-level measurement). For all operator controlled parameters default values are often included that will be used if no other action is taken. This method was applied in the systems described in papers I, IV, and V. In some cases the choice of suitable parameters is an interactive process that may result in time-consuming work for the operator. In that case it may be convenient to store the parameters from one session and use them as default values the next time the system is used. This method was used in paper V.

Many of the run-time parameters are necessary to have available in order to display and interpret the results correctly. Such parameters are often also stored in the result data base for future use.

3.4. Calculations

Except for being sufficiently accurate and reliable, the most important property of the calculations in clinically oriented systems is that they mey be carried out in real time. The main reason for this is the need for the investigator to havealmost instantaneous feedback from the measurement results. Many types of measurements need careful adjustment of the conditions to give clinically useful results which often implies some kind of interaction between the investigator and the measurement system, like in papers I and V. Even if this is not the case, the clinical routine cannot tolerate too slow response, especially not in man-machine interaction. This was of importance in the project reported in paper IV.

For on-line measurements the ideal calculations are those that may be applied to the data in the order they are acquired. This makes it possible to use some of the computer capacity for calculations alrea-

dy during data acquisition and eventually to produce results in the meantime. Even if it is not possible to carry out the whole calculation in this fashion, at least some of it may be finished before all the data have been collected which will reduce final result delay. Papers I and V contain several examples of such calculations.

The possibility of implementing true real time calculations has special importance in the case where the amount of measured data is so large that it is unpractical to store it all. If the calculations may be performed in real time, only a small portion of the most recent data will then have to be stored. This had to be realized for the clinical implementation of the methods described in paper V.

3.5 Real time control

Especially for on-line measurements, real time control is necessary for data acquisition. One way of solving this is to let some external events control the acquisition. Most often, however, the system contains a real time clock which makes it possible to maintain real time control in the software.

One special case of real time considerations in data acquisition is described in paper V. Long sequences of analog data were to be sampled at a high rate and stored in digital form on a magnetic disc without any time gaps. This required a double buffer technique and direct memory access (DMA) transfer to the disc. In that way two separate data transfers could be performed in parallel: interrupt driven sampling into one buffer, and DMA transfer from the other buffer to the disc.

Another aspect of real time control is the need for maintaining several parallel, asynchronous processes without loosing too much time or processor capacity. In a typical measurement system, data acquisition, calculations, result display, and operator communication may preferably be considered being four asynchronous processes that ought to be executed concurrently.

The way of implementing such parallelism in the software entirely depends on what kind of operating system is available. With no operating system available, the real time control will have to include all basic interrupt handling on assembly language level. If some kind of real time operating system is present, however, high level language multitasking facilities may be available. In paper I a version of real time Fortran was used to implement a still higher virtual machine level for real time programming.

3.6 Operator communication

The role of operator communication in a measurement or display system is to provide the operator with convenient means for immediate control of the system. One special part of this communication is the result display which will be discussed separately in the next section.

An important component in most operator communication schemes is a command language in which the operator can easily expres his intentions. All the papers I - V include some sort of such command language, especially elaborated on in papers I, III, and IV.

In paper I some of the command facilities constitute a separate subsystem, executing independently from the rest of the system. The real time control system was then designed to direct any spontaneous command to the appropriate software module for further processing.

When the system contains a graphical display device, it is sometimes convenient to use a graphical cursor as means for the operator to communicate, e.g. by indicating a certain detail in an image for a certain action. Hardware and software facilities for this were included in the systems of papers I, III, and V, but were not needed very much. In paper IV the importance of such a facility is discussed, but in that case it was not available in hardware.

3.7 Graphical result display techniques

In all the papers I - IV the results are presented in graphical or pictorial form. Most of the papers (I - IV) contain results that are adapted for presentation even in topographical form, i.e. as a three-dimensional function that might be presented as an image or a map. In these cases the result display also involved various degrees of image processing.

Papers I, II, and IV contain examples of results of a direct topographical nature, obviously suitable for presentation as some kinds of maps. In paper V, however, the primary data have no obvious relation to topographical presentation. As in many other cases involving large amounts of data, presentation in graphical form anyhow turned out to be the most comprehensive. It was then necessary to organize the data in a way that made it possible to produce an image which, in this case, visualizes an abstract topography with only one variable (time) being a physical quantity.

Using colour displays like in papers I - III is a matter of ever-lasting controversy in medical information systems. In many cases it is more or less a matter of taste, habits, or elegance, to use colour instead of grey-scale presentation. Two exceptions shall, however, be mentioned here.

In papers I and II a relative scale is often used with the baseline in the middle, positive differences towards the top, and negative towards the bottom of the scale. Using appropriate colours, it is then extremely easy to distinguish areas with high relative values from those with low values. In a grey-scale image it is not possible to have two or more subscales that are easily recognizable. In paper III an other example is shown which illustrates the superior ability of our visual system to detect details of coloured patterns compared to grey-scale.

A technical aspect on graphical display technique emphasized in pa-

pers I and IV is the importance of having suitable basic software available when developing program for image processing or display.

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